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DIPG, Pediatric Brain Cancer, and the Importance of H. Res. 114

Congressional Briefing
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Washington DC, 20515

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DIPG, Pediatric Brain Cancer, and the Importance of H. Res. 114

Congressional Briefing

February 13, 2020 at 11am, 2168 Rayburn HOB, Washington DC, 20515

Welcomes you.

In Collaboration with the Office of Congresswoman Jackie Speier

DIPG Advocacy Group is an association of pediatric brain cancer organizations and childhood cancer advocates in support of the National DIPG Awareness Resolution, founded by Janet Demeter (Jack's Angels Inc), Elizabeth Psar (Julia Barbara Foundation), and Paul Miller, childhood cancer advocate, in Sept. 2017.

Written specifically for this event, in his absence:

"As an adoptive parent of a 7-year old girl who died from DIPG, I can state that the courage of the children and families fighting this disease is in sad and direct disproportion to the attention and funding it gets in America. This is a disease that almost always strikes young children, which means, more than most diseases, it robs the future. We must turn our attention and resources to saving children who have barely begun their life journeys.

To be told "there is no cure" is devastating to any patient. When told to kids as young as 3 or 4, it is beyond tragic. DIPG robs our future generations. If we do not dedicate serious funding and research to it right now, we are turning our backs on our most precious resource, our children.

--Mitch Albom

Author, *Finding Chica*

Welcome statement, DIPG Advocacy Group

issued by Janet Demeter, founder of DIPG Advocacy Group, president of Jack's Angels Inc
The live version was unscripted; the following text is supplemental and designed specially for this format.

Thank you all so much for gathering here today to hear the testimony of experts in neuro-oncology, innovators in industry, philanthropy, and Dr. Malcolm Smith from NIH about exciting new developments for pediatric brain cancer at NCI. Most importantly, we'll hear from Jace Ward who is in active treatment for DIPG. Jace is a pre-law student at Kansas State University with top grades; he's willing and able to be a face for DIPG, as more often than not, young children are so diagnosed with too little time among us. This is a rare and precious opportunity to hear from a DIPG patient about the reality of his life.

We are all here because pediatric brain cancer is a horrible killer of children in the United States, and DIPG is the worst of the worst, and because all here would benefit in their work from greater public awareness. Without it, there has been no progress in treating pediatric brainstem glioma since Neil Armstrong's daughter died of it in 1962. **H. Res. 114, the DIPG Awareness Resolution, is our #Moonshot4Kids**. We sent men to the Moon with 1960s technology and brought them back safely, because we wanted to; it was a powerful goal to our national interest, and to the benefit of humankind. Forty years ago, leukemia was a death sentence. But because we targeted it, and called it out by name, we've made great progress with most types of leukemia, mostly from research on adult leukemias with protocols successfully translated for children, prompting many to assert that 4 out of 5 children survive cancer.

The hidden story here is that most exclusively pediatric cancers are deadly, marginalized as rare, as they all have relatively small patient populations, and thus receive inadequate research funding. Although difficult we are requesting your attention to the indescribable human suffering that has gone unnoticed in obscurity for decades, both for the children who must walk bravely toward their death in full cognitive awareness as their bodies decline, and for their loved ones who have no recourse but to witness this tragedy in utter helplessness because, as we so often hear, "the numbers aren't great enough for investors," in the wealthiest country in the world.

Our experts today will attest to this ongoing tragedy which they have personally witnessed, and as forced harbingers of such ill fate; they have devoted their lives to studying the disease and finding treatments for it. With high technological capability, the obvious question is why we have no real solutions yet. The answer is simple: lack of public awareness, awareness among our lawmakers, awareness in the medical community as to the urgency of this need, as the terrible statistics of pediatric brain cancer are lost amid an onslaught of questionable advertisements telling the public that most children survive cancer.

H. Res. 114 is a pleas to our Representatives in Congress for help; it is meant to shine a light on a very dark place where ignoring childhood deaths by cancer has been made acceptable. With the designation of May 17 as an awareness day for DIPG and pediatric brain cancer, as it has been heralded in 32 States in 2019, the United States Senate for 2019, and in perpetuity in the United Kingdom, it creates awareness for doctors to know there are clinical trials worth trying as we seek to move hopeful treatments forward. Awareness gives parents of the diagnosed more knowledge concerning available treatments when a matter of days can mean life or death. We would challenge the world to be aware of the deadly killer of children and know DIPG by name, and to inspire the collaboration of resources toward its cure.

The Resolution also represents a significant opportunity for needed communication between the American People and their Representatives in Congress, such that issues of urgent concern, otherwise unknown, be addressed and recognized by Congress and so the greater public; it provides a uniting measure by which our country might lead in a humanitarian effort. We sincerely hope that the wisdom of Representative Speier of California and David Joyce of Ohio, in their 2019 introduction of the Resolution and the 98 current cosponsors, the many research institutions, private sector supporters and endorsements of H. Res. 114, will help you to keep an open mind about considering lending your signature in support and to attach hope to a place of darkness and suffering in our society today.

Dr. Sabine Mueller, our first speaker, is very special to me personally as she was the conferring expert in 2014 on the very first DIPG Awareness Resolution to pass a state legislature in California of that year. Since then, she has led the charge with the Pediatric Neuro-Oncology Consortium (PNOC), and has led in developing a cutting edge program for brainstem glioma in Zurich Switzerland, which we look forward to hearing more about; welcome, Sabine!

Dr. Sabine Mueller

Adjunct Associate Professor University of California San Francisco Director,
DIPG Centre of Excellence, University Children's Hospital Zurich

- ***Clinical Reality of DIPG, Treatments go Abroad –***

Good morning everyone.

It is a true honor to be here today and support Janet in her tired less fight to create more awareness for children and families whose lives have been changed forever by being told "your daughter/your son has a brain tumor".

As some of you might already be aware, today more children die from a brain tumor compared to any other childhood cancer but unfortunately support for research for pediatric brain tumors remains extremely limited – from federal agencies as well as from industry. Amongst pediatric brain tumors, Diffuse Midline Gliomas including Diffuse Intrinsic Pontine Gliomas (short DIPG) are the deadliest tumors of childhood and there are virtually no long-term survivors. Children often come to attention at a young age after only a few weeks of symptoms: common descriptions include "She was more unsteady and kept falling"; "His eyes did not move correctly anymore…"; "She could not use his left side of his body anymore". …Sooner or later a picture is taken of the brain which often unfortunately leads little doubt about the diagnosis.

When we as neuro-oncologist then meet for the first time with these families – we not only have to tell them that as a community we have not been able to find an effective therapy for these tumors but that the time a family has left with their daughter or son is extremely limited. The median survival for these tumors is only about 9-12 months – for many less than a school year.

And these numbers have not changed significantly over the last decades. The desperation of families trying to save their child and our lack as a medical community to offer better therapies for these deadly tumors, has driven families to seek care outside the US and Europe often putting families in desperate financial and emotional situations with unclear benefit.

But, there is hope – I remain optimistic that with increasing awareness, the right financial support and true collaboration amongst key stake holders such as families, advocacy groups, regulatory agencies and the medical community, we will be able to change the outcome of these tumors.

One big dilemma our field suffered or continues to suffer from is access to tumor tissue from these Diffuse Midline Glioma tumors. Since these tumors are located in midline structures of the brain that control critical function such as breathing, heart rate etc. and grow intertwined with normal brain - a surgical resection is often impossible and for the longest time even taking only a small piece of the tumor was considered "too dangerous". And then the field got caught in a circular argument – "we can only perform a biopsy if that impacts treatment for a child" – but "how can we learn this if we never start looking at the tissue".

Through a lot of advocacy from families and collaborative efforts with the medical community, now biopsies are offered routinely as part of a clinical trial and in some centers such as UCSF and Zurch amongst others as routine standard of care. And we have learned from these studies that taken a biopsy is safe if done in the right setting. However, getting to this point took over 15 years – and our families do not have that time. But it also highlights that we all need to work together to drive progress.

With the collection of tumor tissue we have seen an explosion in research pertaining to these diffuse midline gliomas. The scientific community has discovered key alterations that drive the development of these tumors; this has helped us to understand that despite the similar appearance of these tumors in imaging and their similar clinical course of development, these tumors come in different subtypes – which most likely will require different therapy approaches. Taking tumor tissue has also allowed us to develop animal models that we can use to test new drugs. We are still waiting for these great new discoveries to lead to better outcomes, but our increased understanding of the biology of these tumors will also help us to develop better therapies.

As a community we have to continue to work together and advocate for families and children affected by this terrible disease – it always starts with awareness and this is why this resolution is so critical:

- Increasing awareness will hopefully lead to more groups working together on some of the critical aspects that limit the opening of trials, testing new and promising agents; this takes much too long. Solutions may be found in stronger consideration for international trials and combination therapies; for a rare disease like diffuse midline gliomas, agencies from different countries need to work much closer together and allow for a more seamless regulatory approval process.

- The field needs more industry support and we will hear from Josh Allen from Oncoceutics in a bit – but we in academia cannot solve this problem alone.

- Data sharing/collection remains a key limitation and Dr. Resnick will address this further in his presentation. But the desperation of families leads to expenditure of sometimes several 100,000 US$ for experimental therapies per family that sometimes does not contribute to the larger knowledge in the field since data is not being collected and shared appropriately.

- But one other key issue remains–funding. Most funding for DIPG research comes from dedicated family run foundations such as the ones represented here today. Our dedicated clinical trial consortium to develop new therapies for children with brain tumors " PNOC" or the "Diffuse Midline Glioma Center" in Zurich is only funded by philanthropy that allows us to move quickly and react to new discoveries faster but remains a challenging model for the longterm.

I am hoping for your support and commitment to this, so that there will be a day in the near future when I can say to families, "…This used to be an incurable disease, but through true collaboration we now have effective therapies….".

Thank you.

H. Res. 114 Testimony of Support

Charles Keller MD

Scientific Director, Children's Cancer Therapy Development Institute, cc-TDI.org

-- The 'Valley of Death' in the current medical research industry; the humanitarian and commercial value of research --

Respected Congresswomen and Congressmen, Thank you for the opportunity to speak to an opportunity for you to advocate for your constituents who are too young to have a public voice. The topic today is a childhood brain tumor, diffuse intrinsic pontine glioma (or DIPG). My assignment is to provide objective information on the pre-clinical gap that is a rate-limiting step between the uniform mortality of this childhood cancer and science-justified, hope-filled new treatments.

First let me introduce myself briefly. I am a classically-trained pediatric hematologist-oncologist, continuously funded by the National Cancer Institute for more than 15 years, beginning with my NCI K08 physician-scientist career development award in the laboratory of my mentor, 2007 Nobel laureate Dr. Mario Capecchi. The NIH Pediatric Research Loan Repayment Program made the earliest stages of my focused research career possible. My training phase has been followed by NCI R01 independent extramural academic research funding for over a decade. I am thus a typical example of following the federal childhood cancer research system, although not all of my peers over the years have stayed on this path, either by choice of their own or by the challenge to sustain research funding. My current role is scientific director of a non-profit 501c3 biotech for childhood cancer research and drug development, Children's Cancer Therapy Development Institute, and I recently co-founded a sister for-profit benefit corporation for pediatric cancer drug development, Artisan Biopharma. I am sometimes funded by the pharma industry for small research studies, but most of my valuable interactions with pharma are scientist-to-scientist non-monetary collaborations. I am a believer in the Baye-Dole Act, whose spirit says that inventions should be moved to commercialization to make effective treatments available to patients who need them. I am the inventor of several patents.

Back to the topic at hand: for childhood cancer, the potential for giving back *saving* childhood in the form of durable cures with minimal side effects has never been greater. *But we simply* We are not there yet. We are at a plateau. Every tool of science and engineering we might dream of is at our fingertips. But while *every year* adult cancer research results in 12 or more drugs so effective to extend or save the life of an adult with cancer, for children only 8 drugs have met this criteria since 1978. 12 every year for adults. Only 8 for children in 42 years. Of course, childhood cancer is rare … representing less than 16,000 patients of the more than 1.6 million cancer patients in the US each year. Thus the market incentive is low. Yet government can, and has begun evening the scales. *The humanitarian incentive for America's children is high; cancer is the leading disease-related cause of death in children in the United States, with brain cancer topping the list of killers. Of brain cancers, DIPG claims more children's lives than any other.*

If FDA approvals are to be a measure of progress in pediatric brain tumors, then the two most recent approvals are CCNU (a derivative of mustard gas) in 1976, *(for "Brain tumors, primary and metastatic, following appropriate surgical and/or radiotherapeutic procedures")* and everolimus in 2009 *(for "subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis who require therapeutic intervention but are not candidates for curative surgical resection.")*

No primary drug approvals for a pediatric brain tumor have ever existed since the beginning of time.

The solution is cross-disciplinary collaboration. Congress has already created many tools to make this happen (which I will outline). Now, awareness is the key, making HRes114 very timely.

First, allow me to describe the process of research and this preclinical gap. Basic science discoveries uncover how a cancer like DIPG works. This basic research might also suggest a potential drug to turn off a key cancer mechanism or target. At a minimum, this represents a $400,000 unit of research, and this type of research is favored by NIH and NCI for funding. Clinical trials to test a new drug may cost $10.5M or more, and so putting a drug into a clinical trial needs sufficient justification. NCI also supports cooperative groups of children's hospitals to conduct nationwide childhood cancer clinical trials. The conundrum is that many clinical trials are started with little or no basic science justification, only the knowledge that a new adult cancer drug is available. The clinicians are not wrong to do so – they require additional preclinical research of the basic scientist to ensure that the scientist's target is reproducibly turned off in animal models of a particular childhood cancer – and those animal models must represent the biological diversity for many childhood cancer patients. This unit of research is $200,000 to $500,000 done properly.

NIH and NCI rarely fund extramural research for this preclinical gap. Nevertheless, we have an exciting precedent to share: with private foundation funds, our laboratory coordinated 12 other labs worldwide to validate the basic science and preclinical utility of a drug called panobinostat for DIPG. This work was published in the journal Nature Medicine in May 2015 and featured on the NIH Director's Blog. We appreciate the NIH Director's attention to our work, but only wish that our example was less noteworthy and only one of many instances that a lab would (1) determine how a pediatric brain tumor works, (2) find a drug with a repeatable beneficial effect, and (3) move that drug to a national clinical trial with availability to all children in need.

(pause)

Here is why I am optimistic, and how you can help:

By drawing attention to the pre-clinical gap, and to the urgent need for solutions for children with brain cancer, and DIPG, H. Res. 114 is a straightforward mechanism to stimulating conversation, innovation and potential new cures.

Congress has created a series of carrots and sticks that facilitate pharma-academic collaboration. The Pediatric Priority Review Voucher rewards drug companies that invest heavily in research and development of rare pediatric diseases like cancer to receive a voucher for accelerated review of their next drug. The voucher is transferrable, and thus has a cash value of $30M or more. $30M would fund a lot of new childhood cancer research R&D (5 times more than the Carolyn Pryce Walker Act that allowed me an R01 supplement to increase awareness and support of childhood cancer research). On the other hand, the RACE Act creates an obligation for pharma companies to find and test any potential application(s) of their drugs in pediatric cancers. Both *(of these enacted legislations)* came about by community awareness, community action and legislative advocacy. **The clear reasons for cross-disciplinary collaboration exists, and now we just need to get the word out.** I recently visited a colleague at a pharmaceutical company in New Jersey about licensing a shelved drug to treat a pediatric brain tumor. This internal champion knew nothing about the Voucher incentive or the RACE Act responsibility, and perhaps less about pediatric brain tumors. Awareness can help close this gap.

Thank you for your attention and advocacy on behalf of children touched by DIPG and other cancers, including Jack, Andrew, Caleb, Philomena and my friend Josh.

Josh Allen, Ph.D.

Senior Vice President, Oncoceutics; 2016 Forbes “30 Under 30”
- *The challenges faced by smaller biotech with promising discovery* –

Good morning. My name is Josh Allen. I am Senior Vice President of Research and Development at Oncoceutics.

I discovered ONC201, an investigational therapy that is being developed by Oncoceutics for the treatment of DIPG and other forms of lethal brain cancer with no treatment.

I am also the son of a childhood cancer survivor.

As many of you know, the cancer death rate has been declining in the United States thanks to the tireless efforts of the entire oncology community that have revolutionized the management of some forms of cancer. Some of these cancers that I was taught only 10 years to be incurable diseases are now sent into remission by new therapies. Unfortunately, DIPG is not one of these.

The breakthrough progress that we have witnessed in some cancers is only possible when the full ecosystem is working together: academic researchers, physicians, patients, their families and advocates, regulators, and industry, among others.

For DIPG, the academic researchers have been hard at work making exciting discoveries that help us understand this disease and how to best fight it. The physicians are passionate and highly motivated to do whatever they can to help these patients. The patients, as well their families and advocates are among the most resilient, tenacious, and well organized people who you will ever have the privilege to meet. That leaves regulators and industry, which I am here to discuss.

Oncoceutics is among a very small number of companies who have included DIPG in its development of novel therapies. There are myriad reasons why this group of industry members is so small:

First, clinical trials for drugs to treat brain tumors in general have an extremely high failure rate.

DIPG is even worse….it has seen decades of trials that have uniformly failed to improve survival.

DIPG is considered an extremely rare disease, having an annual incidence of 200-400 patients in the United States; this protracts how long it takes to run clinical trials; it is also very difficult to provide financial justification that the drug discovery and development costs can be recouped in the event of commercial success

This list continues for a very long time, but suffice it to say that there are many reasons why DIPG has not been a priority for the drug development industry.

And yet this must change. We cannot continue to let hundreds of people, many of whom are children, have their lives stolen by DIPG. The good news is that there is cause for hope.

Grant-funded research has breathed new hope into the community. We have only recently begun began to understand what goes wrong in DIPG. This allows us to understand why so many prior therapeutic efforts have failed, and casts light upon on a series of molecular defects. This gives us hope that new therapies could be targeted to those defects to finally make progress in this disease.

Not only is there cause for hope, but there are things that people in this room can do to help.

In the case of Oncoceutics, we would not have been able to discover or develop ONC201 for DIPG without government supported research. We simply would not have known about DIPG and almost every step of the discovery and development has been critically enabled by research supported by NIH and other government agency grants.

Without grant support:

- We simply would not have be able to discover the drug,
- Would not have been able to translate it to the clinic,
- Would not have run brain tumor trials,
- Would not have known that a mutation that is key to making tumors respond to this drug is common in DIPG and certain other kinds of brain tumors.

Private funding was not option, as each of those steps individually carries a long history of failure.

We are eternally grateful for the support that has enabled the discovery and development of ONC201, but how many other promising novel therapies discovered in academic labs never had the chance to be tested in clinical trials? How many more worthy therapeutic ideas will we read about in research journals that will remain trapped in the lab and never reach patients?

I call upon you to increase support for federally funded basic, translational, and clinical research for DIPG, as suggested by House Resolution 114.

This will be critical in allowing regulators and more industry partners to unite with the rest of the DIPG community in doing everything that we can to help these patients live longer and better lives. Let's give these patients, their families, and the community the help and hope that they deserve.

Thank you.

Dr. Malcolm Smith, NIH | DIPG Congressional Briefing February 13, 2020

Associate Branch Chief, Pediatrics in the Clinical Investigations Branch [Cancer Therapy Evaluation Program, Division of Cancer Treatment and Diagnosis], National Cancer Institute

Good morning,

I would like to thank our hosts today, especially Janet Demeter and all of the other families and organizations who have come together to put a spotlight on this issue, to emphasize the need for continued research, and to honor the children we have lost to DIPG and their families and those facing a diagnosis today.

Thank you as well to Congresswoman Speier, for her leadership of the Childhood Cancer Caucus and the Biomedical Research Caucus – and thank you to her and her colleagues for their strong bipartisan support for NCI, NIH, and childhood cancer research.

Thank you for this opportunity to talk about research supported by the National Cancer Institute, and across the National Institutes of Health, to advance progress for children with DIPG.

As many of you know, NIH is the federal government's biomedical research agency, and NCI is one of the 27 Institutes and Centers that make up NIH. NCI and all of NIH are primary supporters of basic biomedical research, and both NCI and the National Institute for Neurological Disorders and Stroke – or NINDS – support research on brain tumors.

My role at NCI involves overseeing a portfolio of large translational and clinical research programs funded by NCI – including the Children's Oncology Group, the Pediatric Preclinical Testing Consortium, the Pediatric Early Phase Clinical Trials Network, and a program that I'll talk about in more detail today – the Pediatric Brain Tumor Consortium, or P-B-T-C.

I'll focus on two major areas of research: first, basic science studies that allow us to better understand the biology of DIPG and other pediatric brain tumors and that we hope will establish a foundation for future clinical progress. And second, I'll describe clinical research programs to evaluate the new therapies and approaches that are needed for children with DIPG.

I'll share examples from NCI, NINDS, and other areas of NIH, so there is a lot of ground to cover in the next five minutes!

Ongoing NIH investments to understand the biology of DIPG have been critical to moving this field forward.

NCI has provided long-standing support to Dr. Suzanne Baker and her outstanding team at St. Jude Children's Research Hospital. Theirs was one of the first groups to report on the histone mutation that is now recognized as a fundamental characteristic of DIPG, and this team is conducting basic and translational studies in an effort to develop effective, relatively non-toxic therapies through a better understanding of the biology of DIPG.

I'd also like to highlight Dr. Michelle Monje's work at Stanford. She has been supported throughout her career by NINDS, and more recently with the NIH Director's Pioneer Award, supported through the NIH Common Fund. The Common Fund is important as a way to address high priority challenges in biomedical research that no single NIH institute can address on their own, and it is also home to the Gabriella Miller Kids First Research Program, in which NCI is a key collaborator.

If you are familiar with Dr. Monje you know she is one of the foremost scientists studying and developing new therapies for pediatric brain tumors like DIPG. Her basic and translational research – supported by NIH and many pediatric brain tumor foundations – has led to NCI-supported clinical trials, both current and in development.

I also want to call your attention to Dr. Davis Allis at Rockefeller University. NIH support to fund basic researchers like Dr. Allis has been critical to advancing our understanding of the molecular drivers of DIPG. Dr. Allis' research on histones, a type of protein that helps package DNA, has been supported by NIH since the 1980s. But it wasn't until histone mutations were discovered as molecular drivers of DIPG in 2012 that we could connect the dots between Dr. Allis's basic research work and pediatric cancers. And now Dr. Allis has become a passionate childhood cancer researcher, with a large NCI grant supporting important studies on the role of histone H3 in driving the development of childhood cancers like DIPG.

Additionally, both NCI and NINDS are funding grants to young investigators, like NINDS support for Dr. Sriram Venneti at the University of Michigan. He's building upon what we already know about histones and their role in DIPG – thanks to researchers like Drs. Allis, Baker, and Monje – to investigate how these mutations can rewire cellular circuitry to sustain uncontrolled tumor growth.

Additionally, through the Cancer Moonshot, NCI is supporting a team of Dr. Resnick's colleagues at CHOP to create a Pediatric Tumor Cell Atlas – an incredibly in-depth map of molecular and cellular changes in tumor cells, the tumor microenvironment, and the immune system. The CHOP team is focusing on three high-risk childhood cancers responsible together for more than 50% of all childhood cancer deaths. One of these cancers is childhood high grade glioma, including tumors with histone H3 mutations, and so the Atlas findings will be highly relevant to DIPG.

We are also working across NIH and across the childhood cancer community to ensure that all of this promising basic science is translated and made available for children in the clinic as quickly as possible.

As an example, NCI and another NIH center known as NCATS, or the National Center for Advancing Translational Sciences, have partnered with Dr. Monje and Dr. Kathy Warren, now at Dana-Farber but previously at NCI in our Pediatric Oncology Branch intramural program, to use preclinical information to improve clinical approaches. The NCATS project involved high-throughput screening of over 2,700 compounds on several DIPG cell lines and identified promising combinations to move to clinical testing.

NCI is also expanding the PBTC this year with an increase in its funding. This will allow the PBTC to add up to six additional sites, and it will also allow the PBTC to increase its organizational capabilities so that it can support more clinical trials. An important part of this expansion includes several efforts focused specifically on DIPG, including a clinical trial based upon Dr. Monje's work, evaluating a drug that inhibits the activity of a protein called ADAM10. The expansion of the PBTC will allow it to expand its clinical research program for DIPG and other pediatric brain tumors and will make its clinical trials more accessible to children and families throughout the country.

In addition to the PBTC, which focuses on early phase trials for children with brain tumors, NCI, in collaboration with Oncoceutics, will soon be launching a trial through NCI's National Clinical Trials Network. It is a partnership between the NCI-funded Children's Oncology Group and one of NCI's adult clinical trials groups, to evaluate radiation plus ONC201 for Children and adults with newly diagnosed gliomas with the H3 K27M mutation. As you heard from Dr. Allen, NCI's Small Business Innovation Research Program played an important part in supporting the development of ONC201, and this Phase II trial aims to build upon that progress.

I am sure I have gone over my time, and I know I have not done justice to all of the promising research NCI and NIH are supporting in this field – but I'll wrap things up, so you can hear from David and Jace. Thank you again to Janet, and all of the families and organizations represented here today.

For those who have lost a child to DIPG, I know that the discoveries we are supporting today are coming too late. Please know that my colleagues and I within NIH and those working throughout the country understand the urgency – for all children with cancer, and particularly for those diagnosed with DIPG, and we look forward to continuing to collaborate with you to keep pushing this field forward as fast as we can.

Thank you.

**As a federal employee, Dr. Smith is not able to take a position on H.Res. 114. He will be providing an update on research supported by the National Cancer Institute and the National Institutes of Health to advance much needed progress for children with DIPG and their families.*

Jace Ward BRIEFING ADDRESS

Junior, Pre-Law, Kansas State University; DIPG Patient, ONC201 Clinical Trial

- *DIPG, the Reality: Speaking for Thousands, DIPG Won't Wait –*

Good Morning. I am one of the many faces of DIPG. May 17th of this year I learned what a Diffuse Intrinsic Pontine Glioma is. As I listened my vision blurred and everything went numb. I think the doctor said something along the lines of aggressive, inoperable, terminal tumor in the center of my brain. The only other thing I learned that day, is that I had an estimated 9 months to live. My life would end one day before I turned 21.

There are no words to correctly explain my thoughts in the months following. I can only tell you that brain surgery doesn't hurt but makes you forget how to walk, and radiation masks are straight out of a nightmare. If you are doing the math, yes, I have (Checks Watch) 4 days to live. In 4 days I will be considered lucky to be alive.

I can't promise I'll be back here next year. Which is exactly why I respectfully ask you to co-sponsor House Res. 114 before you leave for the weekend. DIPG won't wait until this is convenient, DIPG won't wait until we are ready. While we have been "waiting" to take a solid stand, DIPG has been taking the sight, the hearing, the speech, the ability to swallow and eventually the breath of thousands of kids across this country. Cruelest of all, we will always be fully AWARE of the torture we will one day endure by DIPG. You see, our cognitive ability will remain in tact. You hear my urgency, once again I plead, please sponsor House Res 114. Let's celebrate National DIPG Awareness Day together May 17, on the first anniversary of my diagnosis.

Since May I've been telling everyone, I can't die… I'm busy!! It's true, but the real truth is at ALMOST 21, I'm just not ready to face the progression of DIPG. How could any child at an average of 8 years old prepare for this? Most nights I lay awake wondering about all those children on this path before me. I wonder if the older ones ever wondered why despite their parents prayers, and pleas, they could not be saved. I wonder if the younger ones even knew why they were at the doctors. The point is we don't know, because as a nation, we are just not aware. We have failed to hear these children and their families.

Today, if I told you there was a person who had killed 300 - 400 kids every year I would imagine every one of us would go home, hug our families and then turn on the news to watch our government save the day. Well I have gone home, and I HAVE HUGGED MY FAMILY.

DIPG is not rare. It is just rarely talked about. I can't expect you to fix something you don't know about. In the US, pediatric cancer kills more children than any other disease annually. Of those deaths, more than 15% are from DIPG. We need this entire country to be aware of that kind of killer. House Res. 114 is an important step in demanding attention be paid to DIPG when funding public or private research. Awareness will lead to more funding for research and cures.

We can solve immediate life-threatening issues with simple awareness. In my state of Kansas, at the largest research hospital, the director of oncology believes there are just 40 cases of DIPG in the US per year. No, sir, there are at least 7 active cases in Kansas. Jessica, in Wichita, KS was diagnosed in July soon after HS graduation. She did all her doctor recommended which was steroids and radiation. There was no discussion of clinical trials or a biopsy to discuss mutations.

In six months Jessica became wheelchair bound, has double vision, cannot use her hands reliably and blood clots formed in her chest. Steroids have run their course causing disfigurement and weight gain. Jessica watched my interview on local TV in December where she first learned of the drug I am taking. Unfortunately, it is too late for Jessica to start the medicine until she waits for her tumor to progress further. My trial may not have helped Jessica, we'll never know, but she deserved to know her options and participate in that decision. We as humans have failed Jessica.

By the grace of God and the people like those in this room, my mother was able to find a different course of action for me. If you want me to be really honest my hope came from a group of warrior hearted Facebook Moms. That's right… I said it….Facebook. They share their children's experiences with trials and stay up to date with current research. In fact their experiences are the most up to date data available for most trials. These parents rallied for me to receive expanded access to ONC201 when I was too old for the clinical trial and access was closed. They then funded the expanded access with fundraisers for 86 kids last year. They were aware that ONC201 is the best chance I have for my mutation currently. They were aware that 70% of those with DIPG have the same driving mutation and it was responding to a new drug called ONC201.

Because these selfless grieving parents were aware, I am very fortunate. I now take the drug, 5 pills one time a week without many side effects. Maybe it is radiation that currently keeps me symptom free and the tumor will come back with a vengeance soon. Maybe it could be the medication and instead my tumor will remain stable for one or even two years. Possibly more, it is too early to tell. More time to enjoy school, accomplish my goals, hug my friends, and to love my family. Maybe another birthday, or if i'm really lucky, I could graduate college. I am one of very few examples of awareness.

I wasn't supposed to be here today. Awareness, three years ago caused a neurosurgeon to lead the way to safer biopsies, which gave researchers a way to detect tumor mutations, which allowed a new drug company to confirm a brand new type of drug could combat 70% of DIPG tumors just within the last year. Which led to my mom finding a few aware parents who knew more than our doctors about choosing our best course of action from facebook.

My story looks different today because parents who have lost children pleaded with my mother to make awareness her priority because we could not depend on awareness within the medical system. As a nation, we cannot allow ourselves to continue being complacent with our lack of knowledge and awareness, our inability to prioritize DIPG patients have resulted in death after death. Just as previously incurable diseases have shown time and time again, Awareness is a catalyst for a cure.

Please give us one day a year to use the biggest forums we can find to tell people about DIPG in trade for all the years of life this tumor has and will continue to steal. We'll use the day wisely to inform the public, guide patients to new treatments, doctors to centers of excellence, and researchers to data all in an effort to find the cure.

Earlier I said I could not expect you to fix something you don't know about.

Well now you do know and my life is on the line.

No pressure and Thank you.

Jenny Mosier

Executive Director
Michael Mosier Defeat DIPG Foundation

My name is Jenny Mosier, and I am the Executive Director of Michael Mosier Defeat DIPG Foundation.

In September 2014, we learned that our son Michael had DIPG. It was his second week of kindergarten and one week after his 6th birthday.

JULY 8, 2014

AUGUST 24, 2014

SEPTEMBER 25, 2014

OCTOBER 23, 2014

In a flash, our lives were shattered. Doctors told us we could try experimental drugs, but he would likely die within a year. We wanted hope. We told Michael that radiation, needle pokes, and medications that made him sick were all to help him get better. He did everything we asked. But, as expected, nothing worked.

JANUARY 26, 2015

APRIL 6, 2015

MAY 15, 2015

Just weeks after diagnosis, Michael couldn't walk. He took steroids that inflicted horrific side effects, including massive, rapid weight gain. He had double vision. His body became paralyzed – starting on his left side and working its way to his right.
DIPG even stole his smile.

MAY 17, 2015

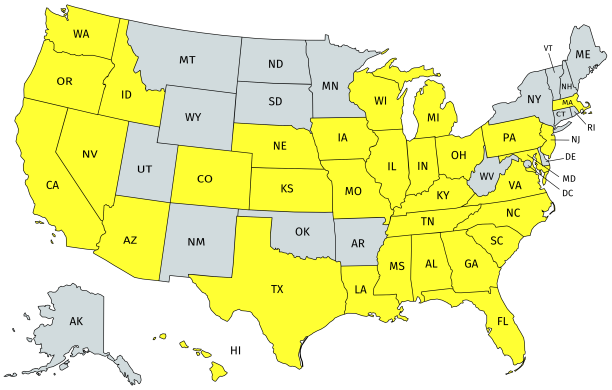
On May 17, 2015, just 8.5 months after diagnosis, Michael passed away.

The first time we heard the term "DIPG" was when Michael was diagnosed. We knew we needed to increase public recognition of DIPG.

We started in our community. In 2016, Governor Hogan established May 17th as the first-ever DIPG Awareness Day in Maryland.

Soon thereafter, I heard from multiple families who wanted to establish DIPG Awareness Day in their state. Other states, including California, Michigan, and Pennsylvania had also recently had DIPG awareness recognitions.

The DIPG community realized that working together, and coalescing around a single date of recognition, would amplify our efforts to make the most impact. And so, the "DIPG Across the Map" initiative began to establish May 17 as DIPG Awareness Day on behalf of all of those affected by DIPG.



DIPG AWARENESS DAY
MAY 17, 2019

32 STATES

In 2019, thanks to the work of many foundations and individuals across the country, **32 states** recognized May 17 as DIPG Awareness Day. We expect more this year, as we the continue this companion effort to the work we are doing on the federal level.

The House of Representatives has the opportunity to stand with thousands of families across the country who have lost children to DIPG, or are fighting right now for their kids' lives.

The burden of fighting for a cure should not fall only on the shoulders of those families who have already paid the ultimate price through the loss of their loved one.

H. Res. 114 alone cannot stop this disease. But recognition by our federal government matters. By raising awareness of this disease, we will build a coalition of supporters who are rallying for our children. Official government recognition of the need for attention and funding for this disease is meaningful as we all work to increase the resources available for researchers.

As DIPG tumors grow, they literally take away the ability for a child to speak. We ask the House to be a voice for our kids through H. Res. 114, by recognizing the importance of their lives, and calling on all Americans to support efforts to find a cure.

Thank you.

Elizabeth Psar

Julia Barbara Psar

Education and Awareness:
The Power to Save Lives Now.

CEO, Julia Barbara Foundation, Knoxville, TN

- Parent Voices -

#Moonshot4Kids National DIPG Awareness Day May 17 2020

Some brain tumors are operable and have greater survivability than DIPG. But with inadequate assessment and diagnosis from the onset of symptoms, we are losing children to brain cancer. "If only I had known," a tearful mother had said to me at one of my foundation events, as her 14-year-old son died in his sleep from a brain tumor, discovered by autopsy. "He'd been complaining of headaches for a few weeks. I had no idea."

Armed with knowledge from our events, friends and extended family have helped others discover pediatric brain tumors before it was too late.

We can save lives today with this Awareness Resolution. Please decide that these children facing certain death are a strong enough case for an Awareness Day.

Thank you.

The Morin Family

"There is no time at all, for some."

The Urgent Need for Awareness.

Luke's Posse, Denver, CO

Luke Morin

- Jill, Cam, and Phebe -

#Moonshot4Kids National DIPG Awareness Day May 17 2020

One day our Lukie was a happy, healthy, energetic and loving boy, and the next we discovered he had DIPG—a death sentence. Luke didn't have a good reaction to radiation therapy, the only standard treatment for DIPG as a temporary fix before progression and death. He endured only 2 treatments and died 17 days after he was diagnosed.

I'd never heard of DIPG; the doctors did, and as I discovered, it's been clinically known since before Neil Armstrong's daughter died of it in '62. Treatments have not changed, nor the prognosis of death in 9 months. We didn't have a chance. No one does, without awareness. No one does, when no one knows to come to the rescue. No one does, when no knows, or cares.

Are we the country where people just look the other way? These are our children. Please recognize the urgent need for help and support H. Res. 114. That is something you CAN do to help.

Thank you.

(-Jill Morin; Phebe was unable to speak, as are most siblings and family members. We who can, carry the message for many, many others you will never hear from.)

Michelle Monje, MD PhD

Associate Professor of Neurology, Stanford University
Scientific Director, Stanford Center for Childhood Brain Tumors

My name is Michelle Monje; I am a pediatric neuro-oncologist at Stanford University. My research laboratory is focused on understanding DIPG, how it arises in the developing brainstem of children and adolescents, what DIPG cancer cells depend on for growth, progression and spread, and how we may best treat it. My clinical research program endeavors to bring what we discover in the lab to clinical trials of new therapeutic strategies for DIPG.

Brain cancer is the leading cause of cancer-related death in children, and DIPG is the leading cause of brain cancer-related death. To date, DIPG is universally fatal, and the average survival is less than a year. It strikes approximately 400 children, adolescents and young adults per year in the United States; given the median age at which DIPG occurs and the average life expectancy in the United States, DIPG accounts for ~24,000 life-years lost annually.

I first became aware of this disease in medical school, when I cared for a little girl with DIPG named Emily, from the day of her diagnosis until her death 6 months later. I was stricken by the unthinkable cruelty of this brain cancer, and stunned by the horrifying realization that, at the time, we knew virtually nothing about DIPG, had no experimental model systems to study it, no knowledge of even the most basic aspects of what drives this seemingly intractable cancer, and – worst of all- no way to even slow down its relentless progression.

In the nearly two decades since her death, motivated by Emily and the ever-growing list of children, adolescents and young adults I have cared for and lost, I have been part of the small but growing team of doctors, scientists and parents fighting to understand, treat and one day cure this terrible childhood cancer. In that time, there has been enormous progress as we have collaboratively developed tools to study DIPG in the lab, uncovered the molecular underpinnings sparking this malignancy, determined ways in which DIPG takes advantage of the rich, growth-enabling environment of the developing childhood brain, and exposed several vulnerabilities of DIPG that we are working to translate to new therapies.

What we are discovering about DIPG has also taught us important lessons about other brain cancers, and has elucidated new possible therapies for more prevalent diseases like glioblastoma.

This progress forward has come only from a collaborative effort that crosses disciplines and borders. It has been supported by those who have seen this disease – through a variety of circumstances - and could not turn away from this urgent unmet need.

How much larger the effort would be, how much quicker we would find effective therapies, if more people were aware, if more people and more resources joined us in this fight. Thank you for taking time to consider this initiative to raise much needed awareness, awareness that will benefit children present and future who face DIPG.

Conclusion

Janet Demeter
Co-founder, DIPG Advocacy Group
President, Jack's Angels Inc, Agua Dulce CA

"Be Resolved."

Angels and Warriors Assemble

H. Res. 114

"YOU HAVE THE POWER."

The Welcome and Conclusion were not scripted; this text is supplemental to the Presentation.

In honor of so many of our children who have faced untimely death with no hope at all, and for all children facing a death sentence today whether from DIPG or other deadly disease, we thank you for considering this **#Moonshot4kids,** H. Res. 114. You must realize the awesome power for good you have, just in a simple signature of support, and we are asking you for your support for this measure today.

You. Have the amazing power of attaching HOPE to pediatric brain cancer with your signature. Why wouldn't you? Do you point to the rules? If ever there were an important reason for exception, wouldn't this be it? Wouldn't we do as a nation everything we could to help? Here is your opportunity; please take it! We can take on any challenge, but success depends upon our being RESOLVED. These kids have no time to lose. Jace has a terrifying, probable end to face, as do many of the very young children before you who have ventured forth in support of this Resolution and the many children who have come before them. Please hear us!

H. Res. 114 is a plea to our Representatives in Congress for help; it is meant to shine a light on a very dark place where ignoring childhood deaths by cancer has been made acceptable. Please help change this! These devoted scientists and officials have committed their lives to saving these children. Please, help us support them.

Thank you.

My Jack, 2 days before he died.

As a founder of DIPG Advoacy Group, I need to publicly thank Mitch Albom for lending his gift of writing to express the importance of awareness for this disease, and also to remind us how important our children are. A whole universe disappears when a child dies, and a family and a community shaken to the core; we are never the same. It's an intensely personal experience which for many does not lend itself to hopeful advocacy in the first years after losing one's child. From our hearts to yours, we thank you Mitch.

"As an adoptive parent of a 7-year old girl who died from DIPG, I can state that the courage of the children and families fighting this disease is in sad and direct disproportion to the attention and funding it gets in America. This is a disease that almost always strikes young children, which means, more than most diseases, it robs the future. We must turn our attention and resources to saving children who have barely begun their life journeys.

To be told "there is no cure" is devastating to any patient. When told to kids as young as 3 or 4, it is beyond tragic. DIPG robs our future generations. If we do not dedicate serious funding and research to it right now, we are turning our backs on our most precious resource, our children.

--Mitch Albom
Author, *Finding Chica*